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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/645,557	08/22/2003	Jhi-Joung Wang	089048-0299	8699

22428 7590 06/11/2007

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EXAMINER	
DESAI, RITA J	
ART UNIT	**PAPER NUMBER**
1625	
MAIL DATE	**DELIVERY MODE**
06/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/645,557	WANG, JHI-JOUNG	
	Examiner	Art Unit	
	Rita J. Desai	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-14 were pending.

Claims 15-21 have been added.

Claims pending now are 1-21.

The rejection of claims 1-21 (previously claims 1-14) rejection under 35 USC 112 written description as failing to comply with the written description has been withdrawn as applicants have amended the claims to put in the C1-C40 aliphatic groups. The specifications on page 16 has the various acids defined on page 16 lines 10-20, which would give the corresponding R group.

The rejection of the claims 1-21 (previously 1-14) under 35 USC 103 obviousness still stands, over

Buchwald et al (J.Med. Chem., 199, 42-5160-5168)

Stinchcomb et al. I Pharmaceutical Reasearch Vol 13 No 10 1996., Vol 12, 1995.

Hu et al US 6225321

Li-Heng Pao 2000 High Performance liquid chromatographic method for the simultaneous determination of nalbuphine and its prodrug, sebacyl dinalbuphine ester, I dog plasma and application to pharmacokinetic studies in dogs.

Applicants argue

The cited references teaches away from the claimed mono-esters. As Stinchcomb I reports that "in no instance did the buprnorphine flux through skin from a prodrug solution exceeds the flus

of buprenorphine base in vivo" .

This is a statement, but it certain does not teach away from the use of prodrugs .

The reference does teach that these esters are 250 times more soluble in oil. The reference also teaches that hydrocortisone 21-alkyl ester prodrug showed evidence of increased hydrolysis rate as the alkyl chain increases see page 1523 .

HU '836 and '321 teaches the long chain esters of nalbuphine (an opioid) have a longer lasting effect.

Applicants further argue that nalbuphine differs from Buprenorphine in 7 different ways.

These compounds are from the same opioid family and have similar properties and structures.

The problem to be solved is that some of the opioids undergoes first pass metabolism causing major inconvenience in clinical therapy. Also the drugs are fast acting and hence do not have a prolonged effect.

According to Pao et al SDN is a synthetic di-ester prodrug which has the same safety profile as the parent.
In conclusion the Pao reference states
" It is reasonable to predict that the conversion of SDN to nalbuphine will be much more rapid in human blood. This prodrug appears to fulfill several criteria proposed by Boder [18]. Basically, no unexpected compound (i.e., a metabolite derived from the non-active part of the prodrug) should be formed in vivo. "

This result implies that the pharmacokinetic properties of nalbuphine converted from SDN in dogs appear to be unchanged. " .
The bioavailability of the prodrug is enhanced as the hydrolysis is enzymetic.

See Hussain Munir et al XP –002238857 1987 shows that the hydrolysis rate is See

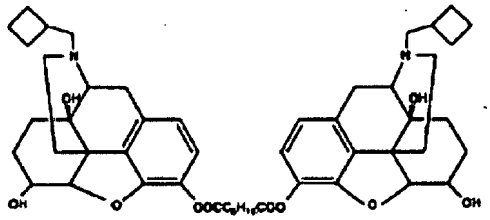
Table I—Hydrolysis Half-Lives of the Anthranilate (2), 3-Acetylsalicylate (3), Benzoate (4), and the Pivalate (5) Esters of Naltrexone (1) in Human and Dog Plasma

Prodrug	Hydrolysis Half-Life, h	
	Human Plasma	Dog Plasma
2	~48[a]	~24[a]
3	0.004[b]	0.08[b]
	0.5[c]	0.6[c]
4	2.0	2.2
5	7.5	2.0

[a] Disappearance was followed for only 24 h. [b] Compound 3 to naltrexone salicylate. [c] Naltrexone salicylate to 1.

Journal of Pharmaceutical Sciences / 357
Vol. 76, No. 5, May 1987

Thus with these studies which are other opioids, one of skill in the art would have motivated to resolve the fast acting nature of the buprenorphine.
When one set of compounds of one family shows a certain property , one of skill in the art would obviously be motivated to use the same to enhance the properties of being longer lasting of other opioids/ analgesics.



Sebacoyl dinalbuphine ester

Pao et al teaches the compounds

It is common sense that familiar items may have obvious uses beyond their primary purposes, and a person of ordinary skill often will be able to fit the teachings of multiple patents together like pieces of a puzzle. Multiple references in the prior art can be combined to show that a claim is obvious. Any need or problem known in the field and addressed by the patent can provide a reason for combining the elements in the manner claimed. To determine whether there was an apparent reason to combine the known elements in the way a patent claims, you can look to interrelated teachings of multiple patents, to the effects of demands known to the design community or present in the marketplace, and to the background knowledge possessed by a person of ordinary skill in the art. Neither the particular motivation nor the alleged purpose of the patentee controls. One of ordinary skill in the art is not confined only to prior art that attempts to solve the same problem as the patent claim. Instruction to the Jury

In **Forgent v. EchoStar: Jury Instruction on Obviousness.**

The obviousness can be implicit and does not have to be confined to same compounds as the instant invention.

Thus in view of the prior art the long lasting property is expected.

Conclusion

Claims 1-21 are rejected.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

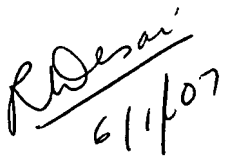
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita J. Desai whose telephone number is 571-272-0684. The examiner can normally be reached on Monday - Friday, flex time..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thomas McKenzie can be reached on 571-272-0670. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Rita J. Desai
Primary Examiner
Art Unit 1625



R.D.
June 1, 2007